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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/699,511	10/31/2003	George Nelson Bennett	61683-00002USPT	3571

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BAKER & MCKENZIE LLP
Pennzoil Place, South Tower
711 Louisiana, Suite 3400
HOUSTON, TX 77002-2716

EXAMINER	
CALAMITA, HEATHER	
ART UNIT	**PAPER NUMBER**
1637	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	12/27/2006	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/699,511	BENNETT ET AL.	
	Examiner	Art Unit	
	Heather G. Calamita, Ph.D.	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on October 27, 2006, has been entered.

Status of Application, Amendments, and/or Claims

2. Claims 1-7 are pending and under examination. All arguments have been fully considered and thoroughly reviewed, but are deemed not persuasive for the reasons that follow. Any objections and rejections not reiterated below are hereby withdrawn.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Watson et al. (Biotechniques, 1997) and Liu et al. (Current Biology, 1998) in view of Stahl et al. (Biotechniques, 1993).

With regard to claim 1, Watson et al. teach a method of assembling PCR fragments comprising (see p. 858 the abstract and p. 860 col. 3 under cloning of lac operon fragment):

a) making a first PCR fragment with first and second primers, wherein the second primer comprises a modified nucleotide that can be removed by a DNA repair enzyme, resulting in a 3' overhang (see p. 858 the abstract and p. 860 col. 3 under cloning of lac operon fragment);

b) treating the first PCR fragment with a DNA repair enzyme to generate a 3' overhang

c) making a second PCR fragment with third and fourth primers, wherein the third and fourth primers each comprises a modified nucleotide that can be removed by a DNA repair enzyme resulting in a 3' overhang (see p. 858 the abstract and p. 860 col. 3 under cloning of lac operon fragment);

d) treating the second PCR fragment with a DNA repair enzyme to generate a 3' overhang (see p. 858 the abstract and p. 860 col. 3 under cloning of lac operon fragment);

e) annealing and ligating the first and second PCR fragments (see p. 858 the abstract and p. 860 col. 3 under cloning of lac operon fragment);

f) optionally repeating steps c, d and e until a last PCR fragment is added to the growing chain to produce an assembled fragment (see p. 858 the abstract and p. 860 col. 3 under cloning of lac operon fragment),

g) circularizing the assembled fragment (see p. 860 col. 3 under cloning of lac operon fragment, where the fragment is circularized in the vector before transformation)

With regard to claim 2, Watson et al. teach one of the PCR fragments comprises an origin of replication and a selectable marker (see p. 860 col. 3 under cloning of lac operon fragment, the lac operon contains a selectable marker and the vector contains an origion of replication).

With regard to claim 3, Watson et al. teach the first PCR fragment or the last PCR fragment comprises an origin of replication and a selectable marker (see p. 860 col. 3 under cloning of lac operon fragment, the lac operon contains a selectable marker and the vector contains an origion of replication).

With regard to claim 5, Watson et al. teach the nucleotide is deoxyuridine and the DNA repair enzyme is Uracil-DNA-glycosylase followed by T4 endonuclease V (see p. 858 first full paragraph under introduction).

With regard to claims 6 and 7 Watson et al. teach the assembled DNA is greater than 30 kb see p. 860 col. 3 under cloning of lac operon fragment where the lac operon and the vector are greater than 30 kb).

With regard to step (a) of claim 1, Watson et al. do not teach using site specific recombination.

With regard to step (g) of claim 1, Watson et al. do not teach circularization with a site specific recombinase.

With regard to steps (a) and (g) of claim 1, Liu et al. teach site specific recombination and circularization occurring simultaneously in a single step, with recombinase (see p. 1301 under results).

One of ordinary skill in the art at the time the invention was made would have been motivated to apply the method of using the cre/lox recombinase system as taught by Liu with the method of DNA assembly as taught by Watson in order to reduce the time and effort associated with restriction mediated DNA assembly. Liu et al. state, "UPS eliminates the use of restriction enzymes and DNA ligase: instead, these functions are both carried out simultaneously by a single enzyme Cre. This relieves the constraints on cloining vectors with respect to DNA sequence and size because the UPS reaction is independent of vector size or sequence. Furthermore, the time-consuming processes inherent in conventional cloning such as the identification of a suitable vector, designing a cloning strategy, restriction endonuclease digestion, agarose gel electrophoresis, isolation of DNA fragments, and the ligation reaction is shortened to a 20 minute UPS reaction (see p. 1307 col. 1 lines 8-19 under Discussion)." It would have been prima facie obvious to apply the cre/lox recombinase system as taught by Liu with the method of DNA assembly as taught by Watson in order to have increased efficiency in assembling DNA fragments. The

use of cre/lox recombinase system provides for rapid and efficient generation and manipulation of recombinant DNA.

With respect to step (b) of claim 1, Watson et al. and Liu et al. do not teach immobilizing the PCR fragments for assembly.

With regard to step (g) of claim 1, Watson et al. and Liu et al. do not teach removing the assembled fragment from the solid support.

Stahl et al. teach immobilizing PCR fragments for assembly (see p. 424 abstract and p. 425 Figure 1).

Stahl et al. teach subsequently removing the assembled gene construct from the bead prior to subcloning (see p. 426 col. 2 first full paragraph).

One of ordinary skill in the art at the time the invention was made would have been motivated to apply the step of immobilizing the fragments for assembly as taught by Stahl with the method of DNA assembly as taught by Watson and Liu in order to have a controlled assembly of the fragments. Stahl et al. state, "Immobilization of the first oligonucleotide enables controlled stepwise annealing/ligation of successive 5' phosphorylated oligonucletides to rapidly build up accurate gene constructs making it possible to sub clone for subsequent expression of the gene product (see p. 424 col. 3 first full paragraph)." It would have been prima facie obvious to apply the step of immobilizing the fragments for assembly as taught by Stahl with the method of DNA assembly as taught by Watson and Liu in order to stabilize and control the assembly of the gene constructs. Controlled assembly yields more accurate gene constructs.

Response to Arguments

4. Applicants' statement on page 4 of the response is read to assert the step of site specific recombination and circularization occurring simultaneously in a single step, with recombinase is inherent

in the claim. The step is therefore necessarily inherent in the reference as the reference teaches the cre-lox recombinase.

Summary

5. No claims were allowable.

Correspondence

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Heather G. Calamita whose telephone number is 571.272.2876 and whose e-mail address is heather.calamita@uspto.gov. However, the office cannot guarantee security through the e-mail system nor should official papers be transmitted through this route. The examiner can normally be reached on Monday through Thursday, 7:00 AM to 5:30 PM.

If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Gary Benzion can be reached at 571.272.0782.

Papers related to this application may be faxed to Group 1637 via the PTO Fax Center using the fax number 571.273.8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to 571.272.0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For more information about the PAIR system, see http://pair-direct.uspto.gov.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Heather Calamita

Art Unit 1637

12/19/2006